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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,400	09/20/2005	Kenji Sato	HOP03167US0	9280

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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,400	SATO ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,11,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10,11,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/18/07, 10/9/07, 11/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2, 4-7, and 12 have been cancelled.

Claims 13 and 14 have been added.

Claims 1, 10 and 11 have been amended.

2. Claims 1, 10, 11, 13 and 14 are under examination.

3. The following Office Action contains NEW GROUNDS of Rejection.

Rejections Withdrawn

4. The rejection of claims 1-12 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's amendment to the claims.

5. The rejection of claims 1-10 and 12 under 35 U.S.C. 102(a) as being anticipated by Murata is withdrawn in view of applicant's declaration.

6. The rejection of claim 11 under 35 U.S.C. 102(e) as being anticipated by Kralovec, et al. is withdrawn in view of applicant's amendment to the claims.

Rejections Maintained/NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 11 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: between steps "f" and "g".

Step f recites a single fraction having 500kDa or more. Since a Sephadex 200 column is used in the fractionation step, the 500kDa fraction would come off the column in a single high molecular weight fraction after the separated fractions because it is larger than 200kDa. Step g recites selection of multiple fractions. It is not clear how the single fraction of step f became multiple fractions in step g.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated proteoglycan composition comprising a gel filtration fraction derived from a water extract of blue shark cartilage with a proteoglycan component of 500kDa or more, the amino acid composition as shown in figure 2 and the method of producing the

proteoglycan composition including the step of correlating MMP-9 and MMP-2 inhibition activity using the assay described in paragraph 96, does not reasonably provide enablement for a proteoglycan composition comprising the amino acid composition shown in figure 2 from just any shark cartilage, or the method of producing the proteoglycan composition including the step of correlating MMP-9 and MMP-2 activity with just any inhibition assay. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The specification discloses isolation of the proteoglycan having a molecular weight of more than 500 kDa and an amino acid composition as shown in figure 2 from a blue shark (page 14, paragraph 88). The specification discloses detection of an MMP-9 inhibition activity by reacting collagen with the proteoglycan composition, a salt buffer solution, and MMP-9 (paragraph 96). The specification does not disclose the amino acid component of the composition

in cartilage from other sharks. The specification does not disclose multiple assays for MMP-9 inhibition.

Hardingham and Fosang (FASEB, 1992. Vol. 6, pages 861-870) teach proteoglycans belong to many different protein families and functions are determined by both the protein core and glycosaminoglycan chains. Gingras, et al. (Anticancer Research, 2001. Vol. 21, pages 145-156, as cited on the IDS) teach inhibition of MMP-9 by shark cartilage extracts using fluorimetric assays and substrate gel zymography.

There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to isolate a proteoglycan composition having the amino acid composition shown in figure 2 from just any shark cartilage or detect an inhibition of MMP-9 with just any assay. The specification does not teach isolation of the proteoglycan composition from just any shark. The specification does not teach more than one assay for detecting MMP-9 inhibition.

In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be necessary to produce the claimed composition and practice the claimed methods wit a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively produce the claimed composition and practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed composition can be isolated from just any shark, commensurate in scope with the claimed invention.

11. Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting MMP-9 activity in blood serum of an animal with pancreatic cancer, does not reasonably provide enablement for inhibiting MMP-9 activity in just any tumor bearing animal or inhibiting cathepsin B activity in a tumor bearing animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The specification discloses treatment of pancreatic cancer by orally administering the isolated shark cartilage extract containing the amino acid composition in figure 2 (example 2). The specification discloses treatment with the shark cartilage extract inhibited MMP-9 activity (paragraphs 119 and 120). The specification discloses haptoglobin has the ability to inhibit cathepsin B and that based on the as-filed data, it is difficult to provide a clear interpretation of the effect on haptoglobin (paragraph 122). The specification does not disclose

treatment of just any cancer with the isolated shark cartilage extract. The specification does not disclose that the shark cartilage extract inhibited cathepsin B activity.

Miller, et al. (Journal of Clinical Oncology, 1998. Vol. 16, pages 3649-3655) teach administration of shark cartilage extracts in patients with advanced cancer was not effective and had little effect on quality of life. Miller, et al. administered the shark cartilage extract to breast, colorectal, lung, prostate, non-Hodgkin lymphoma, and brain cancer patients. Regarding cathepsin B activity, Zwicky, et al. (Biochemical Journal, 2002. Vol. 367, pages 209-217) teach cathepsin B is involved in the destruction of cartilage in osteoarthritis as well as tumor cell invasion and tumor cell apoptosis.

There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to treat just any cancer and to inhibit cathepsin B activity by administering a shark cartilage extract. The specification does not teach treatment of just any cancer. The specification does not teach administration of shark cartilage extract inhibits cathepsin B activity.

In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for treating just any

cancer and inhibiting cathepsin B activity, commensurate in scope with the claimed invention.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Murata (Journal of the Nara Medical Association, 2002. as cited in previous Office Action).

The claims recite an isolated proteoglycan composition comprising a proteoglycan gel filtration fraction, the gel filtration fraction having the following characteristics: a) the gel filtration fraction is derived from a water extract of pulverized shark cartilage; b) the gel filtration fraction has a proteoglycan component with a molecular weight of 500 kDa or more as defined by gel filtration fractionation using Superdex® 200; c) the proteoglycan component of the gel filtration fraction is insoluble in an alcohol; d) the proteoglycan component of the gel filtration fraction has a glycosaminoglycan part mainly composed of chondroitin sulfate C, and e) a protein content of the gel filtration fraction has an amino acid composition as shown in Figure 2. The claims also recite a

pharmaceutical composition, comprising the isolated proteoglycan composition of Claim 1 as an active ingredient.

Murata teaches a water extract preparation of shark cartilage that has a main component of chondroitin sulfate.

Applicant's response filed October 9, 2007 discussed the use of Murata as a 102(b) reference rather than a 102(a) reference (see response page 7). The examiner does not agree with applicant's reasoning for determining the priority date of the application, however, because the Murata reference was published at least one day before the date of the foreign priority document, the Murata reference is available as a 102(b) reference.

Since the claims recite the open language "comprising" when given the broadest reasonable interpretation the claim reads on the shark cartilage extract of Murata and all the limitations of the claim have been met.

13. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Dupont, et al. (US PAT 5,618,925, issued April 8, 1997).

The claim recites a pharmaceutical composition comprising the isolated proteoglycan composition of claim 1 as an active ingredient.

Dupont, et al. teach homogenized shark cartilage in a pharmaceutical composition for the treatment of cancer. Since the claim recites the open language "comprising" when given the broadest reasonable interpretation the claim reads on a crude extract of shark cartilage which would contain the specific

purified isolate of claim 1, therefore, all the limitations of the claim have been met.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The rejection of claims 1, 10, and 11 under 35 U.S.C. 103(a) as being obvious over Murata in view of Kralovec, et al. is maintained.

The response filed October 9, 2007 has been carefully considered but is deemed not to be persuasive. The response state that Murata is not anticipatory of the pending claims (see response page 10). Murata confirms that water extracts of shark cartilage possess MMP-9 and MMP-2 inhibiting properties. Murata further indicates these extracts should be analyzed for the active component(s). Murata speculates the activity is correlated with chondroitin C, either free or bound to proteoglycans, and that the bioavailability of orally administered chondroitin C may explain the reported animal oncology experiments' results (see response page 10). The pending process claim now includes limitations to pulverizing the shark cartilage in liquid nitrogen, partially separating and removing extracted water-soluble components below 6 kDa, and

selecting gel filtration fractions corresponding to estimated molecular weights of 500 kDa or more and correlated with MMP-9 & -2 inhibition activity. None of these limitations are present in Kralovec (see response page 10).

In response to this argument, the Murata reference is available as 102b art as discussed above. Murata teaches an extract of shark cartilage that would be included in the extract of the instant claims because of the open claim language (see 102b above). Murata teaches pulverizing the shark cartilage on dry ice. One of skill in the art would have known to substitute the liquid nitrogen for the dry ice to keep the cartilage sample frozen during the pulverizing steps. Regarding the MMP-9 inhibition activity in the process claim, Murata teaches that water extracts of shark cartilage have MMP-9 inhibition activity and because of the indefinite nature of the determination of MMP-9 activity (see 112, second paragraph, above) it is not clear how the MMP-9 inhibition was determined.

Therefore, after a fresh consideration of the claims and the evidence provided, the rejection is maintained.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

December 5, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER